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The relationship between episodic migraine headache and chronic constipation in adults

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ABSTRACT

Aims: There might be a potential relationship between headaches and constipation. This study aimed to observe the benefits of treating chronic constipation in disease management in patients with episodic migraine (EM).

Methods: Patients diagnosed with EM according to ICHD-3 were recorded according to aura presence/absence, disease duration, frequency of attacks/day/month, severity of attacks (Visual Analog Scale (VAS) assessment) and detailed demographic information and clinical parameters. Of these patients, those with Bowel habit abnormalities (discomfort and bloating in the abdomen, abdominal pain, hard feces, excessive strain during defecation, infrequent defecation and feeling of incomplete emptying) were diagnosed with chronic constipation according to the Rome IV diagnostic criteria during the interiktal period. All participants underwent abdominal ultrasonography and assessed constipation index (CI). Daily 15 cc lactulose syrup and a nutrition program were administered to the EM group with chronic constipation, simple analgesic+prophylactic treatment was administered to EM patients without chronic constipation in severe attacks, and simple analgesic/triptan+symptomatic treatment was administered to patients with mild-moderate attacks.

Results: A total of 106 patients with EM (n=54, 50.9%) chronic constipation and (n=52, 49.1%) non-chronically constipated participated in the study. The relationship between nausea and vomiting (p=0.000), vitamin D levels (p=0.036) and chronic constipation was found to be statistically significant. The difference between pre-and post-treatment USG/CI values, average VAS scores, and pain frequency (day/month) in chronically constipated patients was statistically significant (p=0.000).

Conclusion: This study is important because it shows that medical treatment targeting intestinal transit in patients with EM who have chronic constipation and additional supportive supplements that change dietary habits significantly reduce intestinal volume, which in turn relieves the severity of migraine headaches and reduces their frequency.

Keywords: Chronic constipation, episodic migraine, headache, constipation index

INTRODUCTION

Constipation describes symptoms related to difficulty in evacuation. These include rare bowel motions, firm or lumpy stools, extreme straining, unfinished defecation or a feeling of obstruction, and, in some cases, the utilization of manual maneuvers to ease defecation. Symptoms can be acute, usually lasting less than seven days, and are typically treated with a modification in diet and lifestyle. Chronic constipation is usually described by symptoms lasting at least 3 months.[1] Chronic constipation is a widespread gastrointestinal irregularity with a prevalence of 12.0%–17.0%.[2] The prevalence of constipation has been shown to increase with age generally.[3] The frequency of constipation can reach 33.5% in people over 60 years of age in the community.[4]

Chronic constipation has been reported to cause a vicious cycle of greater than 20% worsening of 15-year survival,[5] decreased daily activity and productivity in the elderly, and frailty.[6,7] Since chronic constipation is associated with many health problems, its diagnosis and treatment are very important. Today, diagnosis is made using the Rome IV criteria.[8,9] After excluding secondary factors that cause constipation, it is recommended that patients boost their fiber and fluid intake, and engage in physical activity.[10]

Migraine is a disease that can be seen with nausea, vomiting, phono-photophobia, and moderate or severe headache attacks lasting between 4 and 72 hours.[11] Migraine is one of the most common types of headaches, affecting approximately 12% of the world's population, and is seen 3 times more in women than men.[12] Migraine is a factor in the workforce's decreased productivity and severe deterioration of quality of life in people's daily work, education, and professions.[13]

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The most common headaches are pain-related suffering and loss of quality of life.[14] Many patients with headaches also complain of constipation.[15] Although the relationship between these two symptoms has not been investigated in detail, it is possible that constipation is critical to the onset of headache and that headache and constipation share a common pathophysiology.[16] Constipation and migraine share pain and discomfort that lead to a decrease in quality of life. Studies are showing that the prevalence of constipation is higher in patients with primary headaches than in the general population.

There might be a potential relationship between headaches and constipation, which has been verified by some studies.[15,16] Since studies in this area are very limited, it is difficult to say for sure that constipation treatment can help improve migraine headaches. However, we noticed that headache symptoms were relieved in some patients after constipation was resolved. Due to the lack of studies in this area, we aimed to investigate the relationship between migraine headaches and constipation in adults and the impact of chronic constipation treatment on improving headache symptoms with this study.

METHODS

This prospective observational case-control study was conducted with approval from the Siirt University Ethics Committee (Date: 23.05.2024, Decision No: 2024/06/01/01-7105) following the Declaration of Helsinki. The study included 54 patients aged 18-70 years with episodic migraine (EM) and chronic constipation in the interictal period and 52 EM patients without chronic constipation. Participants were recruited from the neurology and general surgery outpatient clinics of Siirt Training and Research Hospital in 2024.

EM was defined according to the "International Classification of Headache Disorders, 3rd edition (ICHD-3 beta version)" updated by the IHS in 2013.[17] Although there are no specific diagnostic criteria for EM in ICHD-3, it refers to individuals with headaches less than 15 days per month.[18]

Inclusion Criteria

Patients who did not receive prophylactic treatment in the last month (b blockers, ca channel antagonists, anticholinergic and antidepressants, antiepileptic drugs, hormonal treatments, etc.), those who did not have headaches due to excessive medication use, those who had headaches less than <15 days per month, >5 or more, those who did not have a history of abdominal surgery, and those who did not have a known chronic bowel disorder.

Exclusion Criteria

Hypertension, diabetes mellitus, ischemic chronic heart disease, congestive heart disease, chronic renal failure, chronic liver disease, hypothyroidism and hyperthyroidism, tumors, vascular disease, chronic inflammatory disease, and active psychiatric conditions, neurological diseases causing constipation (CNS and spinal cord lesions), constipating drug use (opiates, antihypertensives, iron preparations, antacids, etc.) and those who had previously received peripheral nerve blockade, botulinum toxin injection, those who had medication overuse headache, worsening of headache during analgesic use, secondary headache, drug intolerance, missing data, those who had abdominal surgery.

Patients diagnosed with EM according to ICHD-3 by the neurologist were recorded of aura/absence, duration of the disease (months), attack frequency/day/month, attack severity (Visual Analog Scale (VAS) evaluation), and detailed demographic information and clinical parameters. VAS was explained to migraine patients for pain severity assessment ranging from 0 (no pain) to 10 (worst pain). Complete blood count, routine blood biochemistry and thyroid function tests, and CRP, vitamin B12, folate and ferritin, and vitamin D levels were measured in all patients. Brain computed tomography (CT) and magnetic resonance imaging (MRI) were performed when necessary to exclude possible secondary causes of headache. Patients diagnosed with EM were randomly referred to the general surgery clinic for chronic constipation questioning, further examination and diagnosis.

EM patients with Bowel habit abnormalities (discomfort and bloating in the abdomen, abdominal pain, hard feces, excessive strain during defecation, infrequent defecation and feeling of incomplete emptying) examined by a general surgery specialist were diagnosed with chronic constipation according to the ROMA 4 diagnostic criteria.[19] According to the ROMA 4 criteria, symptoms must have started at least 6 months ago and at least two complaints must have been present for at least 3 days in the last 3 months. While taking the patient's history, the specialist general surgeon questioned in detail about the duration of his/her symptoms, the frequency of defecation, and whether there were other complaints such as abdominal pain, abdominal bloating, and a feeling of tension in the abdomen, as well as the consistency of the feces, the amount of feces, and whether there was excessive straining during defecation. During physical examination, distention, solidified stool and mass in the colon were investigated. Careful rectal examination was performed. In patients who could not be diagnosed definitively, upper and lower abdominal CT, upper GI endoscopy, and colonoscopy were performed if necessary to exclude secondary causes of chronic constipation.

EM patients with and without chronic constipation, the diameters of the ascending colon (AC), transverse colon (TC), descending colon (DC), sigmoid colon (SC), and rectum (R) were measured with abdominal ultrasonography (USG) on an empty stomach before and after treatment, and the constipation index (CI) [AC+TC+DC+SC+R/5] was evaluated.[20] It should also be noted that there is no general normal reference for the CI, since the definition and measurement of this condition varies from person to person. For this reason, abdominal USG was evaluated before and after treatment according to individual-based diameter changes.

The EM group with chronic constipation was given 15 cc of lactulose syrup daily. A personalized nutrition program (such as a customized diet for obesity, reducing high amounts of tea consumption (»4 cups/day), reducing caffeine consumption, not eating spicy and hot foods, vitamin D supplements, increasing fluid intake, fibrous foods, optimizing other medications used, taking a 30-minute walk daily, etc.) was applied. Additionally, no protective treatment was applied to

this group except for simple analgesics (such as paracetamol) and symptomatic treatment when necessary during attacks.

For EM patients without chronic constipation, simple analgesics+prophylactic treatment (β blockers) were applied in severe attacks and simple analgesics+triptans+symptomatic therapies were used in mild-moderate attacks. After three months of treatment, the number of migraine pain days/month and VAS pain scores before and after treatment were re-evaluated for both groups. Patients with chronic constipation were regularly followed at 4, 8, and 12 weeks by a specialist general surgeon and dietician, and diet programs, personalized nutritional supplements supportive treatments, and medical follow-up were performed for those who were obese. Body-mass index, defecation habits, and diet were questioned in detail again and recorded in the diet clinic. The non-constipated EM group was interviewed again by a neurologist in the headache clinic regarding monthly pain frequency, number of attacks, and pain severity, as well as treatment approach, and controls were performed by phone for patients who could not attend follow-up visits. All analyses were performed according to the treatment-focused principle.

Working Algorithm

*EM diagnosed according to ICHD-3 beta version (interictal period) (n=356)

Exclusions (n=124)
- Prophylactic treatment within the last 1 month
- More than >15 days per month, less than <5 attacks
- Excessive drug use headache (according to ICHD-3)
- Peripheral nerve blockade, botulinum toxin injection
- Chronic systemic and inflammatory diseases, endocrine disorders, active psychosis, CNS and spinal cord diseases,
- Use of anticholinergic and chronic constipation drugs (such as CA channel blockers, B blockers, iron prep etc.)
- Findings supporting secondary headache in neuroimaging
- Lack of data

Evaluation of all EM patients in terms of chronic constipation in the general surgery clinic (Anamnesis, physical examination and necessary examinations) (n=232)
Chronic constipation according to ROMA 4 criteria?

Exclusions (n=126)
- IBS, chronic inflammatory bowel disease.
- Previous abdominal surgery, hernia, incision scarring
- Non-functional bowel diseases

- Chronic constipation according to ROMA 4 criteria? (n=106)

• EM patients with chronic constipation according to ROMA 4 criteria (n=54)	• EM patients who are not chronically constipated according to ROMA 4 criteria (n=52)

- Both groups were treated before treatment (at the time of first admission and diagnosis) and after (at the end of the treatment at the 3rd month) examination of CI [AC+TC+DC+SC+R/5) with abdominal USG and calculation of diameter variability
- Comparison of pain intensity (vas) and pain frequency (days/month) at the 3rd month of treatment with the baseline in both groups

Statistical Analysis

The normality assumption of continuous variables was tested using Kolmogorov-Smirnov and Shapiro-Wilk tests. The homogeneity assumption of variances was tested using the Levene homogeneity test. Descriptive statistics of variables were given as arithmetic mean±standard deviation, median (min-max), and frequencies as n (%). The study's continuous quantitative variables were analyzed using the Independent t-test, Mann-Whitney U test, and Wilcoxon Signed Rank test according to the fulfillment of assumptions. The Chi-square test (Continuity Correction) analyzed categorical variables, considering the expected values. $p<.05$ was considered statistically significant throughout the study. The statistical analyses of the study were performed using R (Version 4.4.1, R Foundation for Statistical Computing) and JASP (Version 0.19.0, University of Amsterdam, Netherlands.

RESULTS

As shown in **Table 1**, a total of 106 EM patients, 54 (50.9%) chronically constipated and 52 (49.1%) non-chronically constipated, participated in this study. 92 (86.8%) of the patients were female and 14 (13.2%) were male. The distribution of genders into groups was homogeneous (p=0.349). The distribution of age into groups was homogeneous (p=0.149). The relationship between nausea and chronic constipation was statistically significant (p=0.000). Nausea was present in 49 (90.7%) of the chronically constipated patients. Nausea was detected in 22 (42.3%) of the non-chronically constipated patients. Nausea was more common in chronically constipated patients. The relationship between vomiting and chronic constipation was statistically significant (p=0.000). Vomiting was present in 26 (48.1%) of the chronically constipated patients. Vomiting was detected in only 2 (3.8%) of the patients without chronic constipation. Vomiting is more extensive in patients with chronic constipation.

Descriptive statistics and group comparison results of quantitative variables of chronic constipated and chronic non-constipated patients are summarized as shown in **Table 2**. According to these results, the difference between the groups

Table 1. Categorical variables

	No chronic constipation n=52 (49.1%)	Chronic constipation n=54 (50.9%)	p#
Gender			
Female	43 (82.7%)	49 (90.7%)	0.349
Male	9 (17.3%)	5 (9.3%)	
Nausea			
No	30 (57.7%)	5 (9.3%)	0.000
Yes	22 (42.3%)	49 (90.7%)	
Vomiting			
No	50 (96.2%)	28 (51.9%)	0.000
Yes	2 (3.8%)	26 (48.1%)	

#: Chi-square test (Continuity Correction)

in terms of vitamin D values was found to be statistically significant (p=0.036). Vitamin D values of chronically constipated patients were found to be lower. The difference between the groups in terms of other variables whose descriptive statistics are given in **Table 2** is not statistically significant (p>0.05).

Table 2. Comparison of variables between episodic migraine groups with and without chronic constipation

	No chronic constipation n=52	Chronic constipation n=54	p
Age	34.83±12.54 31.50 (18.0-70.0)	37.96±12.51 36.00 (18.00-70.00)	0.149&
BMI	29.58±6.74 30.45 (18.40-39.20)	31.73±5.26 32.75 (19.80-40.00)	0.158&
Hb	13.01±1.57 12.65 (9.60-17.20)	12.68±1.56 12.60 (9.30-16.80)	0.279*
WBC	7.29±1.92 7.10 (4.2-12.4)	7.16±1.97 6.80 (4.1-12.2)	0.741*
Platelet	295.00±61.84 294.00 (143.0-450.0)	289.20±71.54 279.50 (146.0-494.0)	0.399&
CRP	3.56±2.44 2.70 (0.5-11.7)	3.05±1.44 2.60 (1.2-7.8)	0.624&
Ferritin	34.04±38.84 20.45 (2.4-191.4)	28.18±43.96 13.20 (2.2-289.0)	0.077&
B12	322.42±81.53 317.0 (182.0-504.0)	321.76±97.22 296.5 (163.0-609.0)	0.719&
Fol	8.69±1.68 8.75 (5.30-12.90)	8.88±1.69 9.15 (4.40-11.90)	0.560*
TSH	1.54±1.06 1.30 (0.10-6.50)	1.59±1.19 1.40 (0.50-8.30)	0.718&
Vitamin D	15.59±10.34 12.10 (4.70-50.10)	12.69±9.43 8.80 (4.20-41.20)	0.036&
Disease duration	1.65±0.48 2.00 (1-2)	1.61±0.49 2.00 (1-2)	0.796&

*Independent T testi, &: Mann-Whitney U, BMI: Body-mass index, Hb: Hemoglobin, WBC: White blood cell, CRP: C-reactive protein, TSH: Thyroid-stimulating hormone

Descriptive statistics and comparison results of USG/CI, pain intensity (vas) and pain frequency variables before and after constipation treatment are given as shown in **Table 3**. The difference between USG/CI values before and after treatment in the chronically non-constipated migraine group is not statistically significant (p=0.645). On the other hand, the difference between USG/CI values before and after treatment in chronically constipated migraine patients is statistically significant (p=0.000). The USG/CI values of chronically constipated patients decreased significantly after treatment. The difference between the VAS scores before and after treatment in the chronically non-constipated group is not statistically significant (p=0.054). On the other hand, the difference between the VAS scores before and after treatment in chronically constipated patients is statistically significant (p=0.000). The VAS scores of chronically constipated patients decreased significantly after treatment.

The difference between the pain frequency (days/month) before and after treatment in the chronically non-constipated group is not statistically significant (p=0.730). On the other hand, the difference between the average vas before and after treatment in chronically constipated patients is statistically significant (p=0.000).

The USG CI values, average vas, and pain frequency (days/month) of chronically constipated EM patients decreased significantly after treatment compared to before treatment as shown in **Figure**.

DISCUSSION

The exact pathogenesis of migraine has not been fully elucidated and depends on many factors, the gut-brain axis being one of them.[21] The term gut-brain axis refers to the reciprocal relationship between the GI tract and the central nervous system (CNS). Functional disorders occurring in this axis have been shown to play an effective role in migraine, multiple sclerosis, mood and anxiety disorders, Alzheimer's disease, and Parkinson's disease.[22,23] Migraine is widespread worldwide, and recent studies have shown that the incidence of migraine is increasing in people with GI tract diseases.[24] Migraine is associated with GI tract disorders such as diarrhea, constipation, dyspepsia, gastroesophageal reflux disease, celiac disease, *Helicobacter pylori* infection, and inflammatory bowel diseases.[25] A study has suggested that constipation is a significant factor in the development of headaches and that these two diseases may have a common pathophysiology.[16] Serotonin (5-hydroxytryptamine) is very important in the pathophysiology of these two diseases.[26] It has also been shown that patients with migraine and constipation have a higher rate of mental disorders.[27]

Research has shown that bidirectional brain-gut interactions play a role in regulating bowel function in both healthy and diseased states.[28] The role of the CNS in modulating various functions of the gastrointestinal tract, including motility, secretion, blood flow, and gut-related immune function in response to psychological or physical stress factors is well known.[29] Reciprocal signaling between the gut and CNS, such as the effect of mucosal inflammation on nociceptive responses, has been extensively investigated.[30] We suggest that headache and constipation might be a result of bidirectional brain-gut interactions.

When we look at the CI determined by abdominal USG before and after cure in people with EM, it was revealed that it decreased statistically significantly. When we look at the literature, in the study conducted by Manabe et al.,[20] CI was shown to be statistically substantially higher in patients with chronic constipation, and these results supported our study.

Table 3. Comparison of CI, pain intensity (vas) and pain frequency (day/month) in the episodic migraine groups with and without chronic constipation before and after treatment

Groups	USG (CI)			Pain intensity (vas)			Pain frequency (day/month)		
	Before	After	p[&]	Before	After	p[&]	Before	After	p[&]
No chronic constipation	28.94±6.83 28.20 (16.0-42.0)	29.86±7.30 29.80 (17.5-56.6)	0.645	7.42±1.37 7.00 (4-10)	7.19±1.52 7.00(3-9)	0.054	8.50±2.32 9.00 (4-14)	8.33±2.51 9.00 (3-15)	0.730
Chronic constipation	30.91±8.75 30.2 (16.4-53.6)	24.03±6.74 23.50(13.0-49.4)	0.000	7.85±1.28 8.0 (5-10)	4.76±1.15 5.0 (2.0-9.0)	0.000	9.26±2.74 9.0 (4-14)	4.61±1.79 4.0 (1-9)	0.000

&: Wilcoxon signed rank test, USG: Ultrasonography, CI: Constipation index

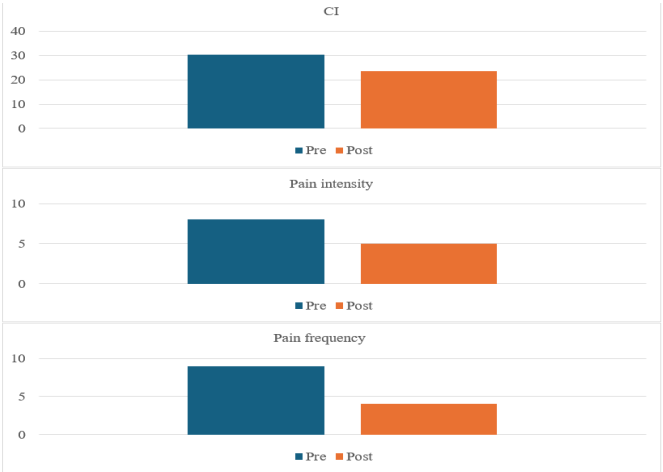

Figure. Comparison of CI, pain intensity and pain frequency variability before and after treatment in episodic migraine patients with chronic constipation
CI: Constipation index

In our study, the relationship between nausea, vomiting, vitamin D deficiency, and chronic constipation was found to be statistically important. The study conducted by Panarese et al.[31] showed a significant relationship between vitamin D deficiency and chronic constipation. Several studies have also shown that serum vitamin D values might be associated with a raised risk of migraine headaches.[32,33] It has been shown that serum vitamin D levels may be lower in patients with migraine headaches than in individuals without headaches.[33] Additionally, vitamin D intake is effective in decreasing the intensity and frequency of migraine attacks.[33]

There are different treatment approaches for constipation. Laxatives may be helpful for those on an inadequate oral diet and soften the stool. In our study, the fact that there was a significant improvement in headache parameters after approximately 12 weeks of disciplined treatment approaches for patients diagnosed with EM and chronic constipation was quite crucial in terms of showing that treating chronic constipation has a significant contribution to migraine and may have an effect on alleviating the symptoms of this disease and may decrease the intensity of pain and invalidity caused by the disease. When the literature was reviewed, the relationship between migraine and constipation was investigated by Rezaeiashtiani et al.,[12] and it was revealed that the intensity of VAS pain caused by migraine decreased with the treatment of constipation. In a study conducted by Inaloo et al.,[15] the association between headache and constipation was evaluated. It was shown that there was a significant association between headaches caused by psychiatric causes affecting mood, such as stress and anxiety, and constipation. Similarly, in the study conducted by Park et al.[16] on headache with constipation, it was revealed that the decrease in headache severity in patients treated for constipation was statistically significant. The findings of our study are parallel to the literature.

Limitations

Being a single-center study, the fact that the study results were evaluated after a 3-month follow-up caused incomplete data, non-compliance with the given treatment protocol, and withdrawal from the study. In addition, including different personalized nutrition programs in this study created difficulties in maintaining the diet strategy in the long term, ensuring compliance with the regimen, and conducting the survey.

More comprehensive, long-term, multicenter studies can be performed in this area, including more patient groups. The current data in the EM group are preliminary and should be interpreted cautiously.

CONCLUSION

EM patients with GI dyspeptic complaints should be questioned for chronic constipation before any preventive treatment plan is made. It has been shown with abdominal USG and supported by CI that in this patient group, treatment with chronic constipation caused an important alleviation in the intensity of migraine headaches and a substantial decrease in the frequency of pain. Thus, relieving patients from unnecessary preventive treatment burdens and preventing the pain from passing to the chronic phase is possible.

ETHICAL DECLARATIONS

Ethics Committee Approval

This prospective observational case-control study was conducted with approval from the Siirt University Ethics Committee (Date: 23.05.2024, Decision No: 2024/06/01/01-7105).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure
The authors declared that this study has received no financial support.

Author Contributions
All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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